Insmed Announces Topline Results from Phase 1 Study of Treprostinil Palmitil Inhalation Powder (TPIP)

--TPIP Generally Safe and Well Tolerated in Healthy Volunteers--
--TPIP Showed Substantially Lower Cmax and Longer Half-Life than Currently Available Inhaled Treprostinil Therapy--
--Pharmacokinetic Profile Supports Continued Development with Once-Daily Dosing--
--Conference Call to be Held at 8:30 a.m. ET Today to Discuss Results--

BRIDGEWATER, N.J., Feb. 19, 2021 /PRNewswire/ -- Insmed Incorporated (Nasdaq:INSM), a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases, today announced topline results from the Phase 1 study of treprostinil palmitil inhalation powder (TPIP) in healthy volunteers. Data from the study demonstrated that TPIP was generally safe and well tolerated, with a pharmacokinetic profile that supports once-daily dosing. A conference call will be held today, February 19, 2021, at 8:30 am ET, with Insmed management to further discuss these results and provide an update on the planned development pathway for TPIP.

"We are very pleased to share these encouraging Phase 1 results, which we believe validate several critical aspects of the TPIP profile and continue to build on the momentum of our earlier preclinical work," said Martina Flammer, M.D., MBA, Chief Medical Officer of Insmed. "Importantly, these findings support the continued development of TPIP with once-daily dosing in a clinical trial program for patients with pulmonary arterial hypertension (PAH). This is a serious, progressive, and rare disease in which the current standard of care is limited by tolerability issues and a cumbersome dosing regimen."

The Phase 1 study of 42 healthy volunteers was designed to assess the safety, tolerability, and pharmacokinetics of TPIP in the setting of single-dose and multiple-dose administration. The highest dose tested as a single dose was 675 µg, and the highest dose tested in repeated dosing was 225 µg.

The study demonstrated that TPIP was generally safe and well tolerated. The most common adverse events (AEs) across all cohorts in the study were cough, dizziness, headache, and nausea. Most AEs were mild in severity and consistent in nature with those typically seen with other inhaled prostanoid therapies. There were few moderate AEs and no severe or serious AEs. Subjects in the multiple dose panel that incorporated an up-titration approach beginning at 112.5 µg once-daily and progressing to 225 µg once-daily reported fewer AEs compared to the panel dosed with 225 µg once-daily from the first dose.

Overall pharmacokinetic results demonstrated that treprostinil exposure (AUC and C_{max}) was dose-proportional, with low to moderate inter-subject variability. Treprostinil was detected in the plasma at 24 hours at all doses and throughout the 48-hour sampling period for the two highest doses. Compared with currently available inhaled treprostinil therapy, TPIP showed substantially lower C_{max} and longer half-life.

Insmed plans to present full data from this study at an upcoming medical meeting.

"The positive results from this Phase 1 study provide clear support for advancing TPIP to the next stage of clinical development in PAH as well as exploring its potential in other serious pulmonary disorders," said Will Lewis, Chair and CEO of Insmed. "These findings represent a significant step toward unlocking the full potential of prostanoid therapy. With continued development of TPIP, we look forward to evaluating whether this novel treatment candidate may offer the potential for improved tolerability, dosing convenience, and efficacy for patients with PAH."

Insmed plans to advance the development of TPIP with two studies in patients with PAH. The first is an open-label, proof-of-mechanism study to understand the impact of TPIP on pulmonary vascular resistance (PVR) over a 24-hour period. The Company anticipates sharing topline data from this study in the second half of 2021. The

second will aim to investigate the effect of TPIP on PVR and 6-minute walk distance over a 16-week treatment period using an up-titration, once-daily dosing schedule. The Company plans to initiate this trial in the fourth quarter of 2021.

Beyond PAH, Insmed continues to explore potential development pathways for TPIP in patients with pulmonary hypertension associated with interstitial lung disease (PH-ILD) and idiopathic pulmonary fibrosis (IPF), and plans to initiate a study in patients with PH-ILD using an up-titration, once-daily dosing schedule.

About the TPIP Phase 1 Study

The Phase 1 study was intended to assess the safety, tolerability, and pharmacokinetics of TPIP in healthy volunteer subjects in the setting of single-dose and seven-day, multiple-dose administration. Serial cohorts of subjects were enrolled. In the first panel, subjects were randomized to receive single doses of 112.5 µg, 225 µg, or 450 µg of TPIP. In the next panel, subjects were randomized to receive single doses of 675 µg of TPIP or placebo.

In the next panel, which was the first multiple-dose panel, subjects were randomized to receive 225 µg of TPIP once-daily for seven days, or matching placebo. The final cohort incorporated a placebo-controlled, up-titration approach in which subjects began at 112.5 µg once-daily for four days, then advanced to 225 µg once-daily for three days.

Conference Call

Insmed will host a conference call today beginning at 8:30 a.m. ET. Shareholders and other interested parties may participate in the conference call by dialing (833) 340-0284 (domestic) or (236) 712-2425 (international) and referencing conference ID number 1963113. The call will also be webcast live on the Company's website at www.insmed.com.

A replay of the conference call will be accessible approximately two hours after its completion through March 21, 2021 by dialing (800) 585-8367 (domestic) or (416) 621-4642 (international) and referencing conference ID number 1963113. A webcast of the call will also be archived for 90 days under the Investor Relations section of the company's website at www.insmed.com.

About TPIP

Treprostinil palmitil inhalation powder (TPIP) is a dry powder formulation of treprostinil palmitil, a treprostinil prodrug consisting of treprostinil linked by an ester bond to a 16-carbon chain. Developed entirely in Insmed's laboratories, TPIP is a potentially highly differentiated prostanoid being evaluated for the treatment of patients with PAH and other rare and serious pulmonary disorders. TPIP is administered in a capsule-based inhalation device. TPIP is an investigational drug product that has not been approved for any indication in any jurisdiction.

About Insmed

Insmed Incorporated is a global biopharmaceutical company on a mission to transform the lives of patients with serious and rare diseases. Insmed's first commercial product is a first-in-disease therapy approved in the United States and the European Union to treat a chronic, debilitating lung disease. The Company is also progressing a robust pipeline of investigational therapies targeting areas of serious unmet need, including neutrophil-mediated inflammatory diseases and rare pulmonary disorders. Insmed is headquartered in Bridgewater, New Jersey, with a growing footprint across Europe and in Japan. For more information, visit www.insmed.com.

Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties. "Forward-looking statements," as that term is defined in the Private Securities Litigation Reform Act of 1995, are statements that are not historical facts and involve a number of risks and uncertainties. Words herein such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "intends," "potential," "continues," and similar expressions (as well as other words or expressions referencing future events, conditions or circumstances) may identify forward-looking statements.

The forward-looking statements in this press release are based upon the Company's current expectations and beliefs, and involve known and unknown risks, uncertainties and other factors, which may cause the Company's actual results, performance and achievements and the timing of certain events to differ materially from the results, performance, achievements or timing discussed, projected, anticipated or indicated in any forward-looking statements. Such risks, uncertainties and other factors include, among others, the following: failure to obtain, or delays in obtaining, regulatory approvals for ARIKAYCE outside the U.S. or European Union (EU), including the United Kingdom as a result of the United Kingdom's exit from the EU, or for the Company's

product candidates in the U.S., Europe, Japan or other markets; failure to successfully commercialize ARIKAYCE, the Company's only approved product, in the U.S. or the EU (amikacin liposome inhalation suspension and Liposomal 590 mg Nebuliser Dispersion, respectively), or to maintain U.S. or EU approval for ARIKAYCE; business or economic disruptions due to catastrophes or other events, including natural disasters or public health crises; impact of the novel coronavirus (COVID-19) pandemic and efforts to reduce its spread on the Company's business, employees, including key personnel, patients, partners and suppliers; the risk that brensocatib does not prove to be effective or safe for patients in ongoing and future clinical studies, including the ASPEN study; the risk that TPIP does not prove to be effective or safe for patients in ongoing and future clinical studies; uncertainties in the degree of market acceptance of ARIKAYCE by physicians, patients, third-party payors and others in the healthcare community; the Company's inability to obtain full approval of ARIKAYCE from the U.S. Food and Drug Administration, including the risk that the Company will not timely and successfully complete the study to validate a patient reported outcome tool and the confirmatory post-marketing clinical trial required for full approval of ARIKAYCE; inability of the Company, PARI Pharma GmbH (PARI) or the Company's other third-party manufacturers to comply with regulatory requirements related to ARIKAYCE or the Lamira® Nebulizer System; the Company's inability to obtain adequate reimbursement from government or third-party payors for ARIKAYCE or acceptable prices for ARIKAYCE; development of unexpected safety or efficacy concerns related to ARIKAYCE or the Company's product candidates; inaccuracies in the Company's estimates of the size of the potential markets for ARIKAYCE or its product candidates or in data the Company has used to identify physicians, expected rates of patient uptake, duration of expected treatment, or expected patient adherence or discontinuation rates; the Company's inability to create an effective direct sales and marketing infrastructure or to partner with third parties that offer such an infrastructure for distribution of ARIKAYCE or any of the Company's product candidates that are approved in the future; failure to obtain regulatory approval to expand ARIKAYCE's indication to a broader patient population; failure to successfully conduct future clinical trials for ARIKAYCE, brensocatib, TPIP and the Company's other product candidates due to the Company's limited experience in conducting preclinical development activities and clinical trials necessary for regulatory approval and its potential inability to enroll or retain sufficient patients to conduct and complete the trials or generate data necessary for regulatory approval, among other things; risks that the Company's clinical studies will be delayed or that serious side effects will be identified during drug development; failure of third parties on which the Company is dependent to manufacture sufficient quantities of ARIKAYCE or the Company's product candidates for commercial or clinical needs, to conduct the Company's clinical trials, or to comply with agreements or laws and regulations that impact the Company's business or agreements with the Company; the Company's inability to attract and retain key personnel or to effectively manage the Company's growth; the Company's inability to adapt to its highly competitive and changing environment; the Company's inability to adequately protect its intellectual property rights or prevent disclosure of its trade secrets and other proprietary information and costs associated with litigation or other proceedings related to such matters; restrictions or other obligations imposed on the Company by its agreements related to ARIKAYCE or the Company's product candidates, including its license agreements with PARI and AstraZeneca AB, and failure of the Company to comply with its obligations under such agreements; the cost and potential reputational damage resulting from litigation to which the Company is or may become a party, including product liability claims; the Company's limited experience operating internationally; changes in laws and regulations applicable to the Company's business, including any pricing reform, and failure to comply with such laws and regulations; inability to repay the Company's existing indebtedness and uncertainties with respect to the Company's ability to access future capital; and delays in the execution of plans to build out an additional third-party manufacturing facility approved by the appropriate regulatory authorities and unexpected expenses associated with those plans.

The Company may not actually achieve the results, plans, intentions or expectations indicated by the Company's forward-looking statements because, by their nature, forward-looking statements involve risks and uncertainties because they relate to events and depend on circumstances that may or may not occur in the future. For additional information about the risks and uncertainties that may affect the Company's business, please see the factors discussed in Item 1A, "Risk Factors," in the Company's Annual Report on Form 10-K for the year ended December 31, 2019, the Company's Quarterly Reports on Form 10-Q for the quarters ended March 31, 2020, June 30, 2020 and September 30, 2020, and any subsequent Company filings with the Securities and Exchange Commission (SEC).

The Company cautions readers not to place undue reliance on any such forward-looking statements, which speak only as of the date of this press release. The Company disclaims any obligation, except as specifically required by law and the rules of the SEC, to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements.

Contact:

Investors:

Eleanor Barisser
Associate Director, Investor Relations
Insmed
eleanor.barisser@insmed.com

Media:
Mandy Fahey
Senior Director, Corporate Communications
Insmed
(732) 487-7468
amanda.fahey@insmed.com

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